

whole brain, olfactory bulb, cerebral cortex, hippocampus, hypothalamus, thalamus, cerebellum, pituitary, liver, kidney and heart were probed with cDNA inserts from the indicated clones. A cyclophilin probe was included in the series as a control for comparable blot loading and RNA integrity. The two hypothalamus samples represent inadvertent mixtures of approximately equal parts of hypothalamus and striatum. The expression patterns are grouped into four classes (A,B,C,D). Only the regions of the blots containing the hybridized signal are shown.

[0014] FIG. 4 depicts the expression patterns analyzed by in situ hybridization, showing coronal sections of rat brains hybridized with single stranded RNA probes corresponding to the inserts of A, clone 35; B, clone 6; C, clone 10; D, clone 20; E, clone 29 and F, clone 21.

[0015] FIG. 5 shows a comparison of rat and mouse cDNA and amino acid sequences corresponding to clone 35 and the amino acid sequence of the peptide hormone secretin. A. The amino acid sequence is listed on the top line, the rat nucleotide sequence on the second line and the mouse nucleotide sequence is listed on the third line. Differences in nucleotide sequences are indicated by asterisks below each different base, amino acid differences are indicated by alternatives (rat/mouse) listed above the encoding triplets. Tandem basic amino acids (putative sites for proteolytic maturation) are indicated in bold italics, as is the serine residue most likely to represent the end of the secretion signal. B. Alignment of hcr1 and hcr2 amino acid sequences with the amino acid sequence of secretin. The first 9 amino acid residues of secretin have been repeated to indicate apparent circular permutation. The identities between the hypocretins and members of the glucagon/vasoactive intestinal polypeptid/secretin family (H. -C. Pehmann, R. Goke, B. Goke, *Endocrine Reviews*, 16, 390 (1995)) are indicated by asterisks; the hcr1 and hcr2 consensus residues appear above the alignment.

[0016] FIG. 6 shows the cDNA and amino acid sequence of clone 29.

[0017] FIG. 7 is a graphical representation of the results of voltage clamp experiments on isolated in vitro rat hypothalamic cells, in which application of 1 μ g hcr2 produced electrical responses in adult but not immature neurons.

DETAILED DESCRIPTION OF EMBODIMENTS

[0018] The following definitions are set forth to illustrate and define the meaning and scope of the various terms used to describe the invention herein. All patents and other publications mentioned in this specification are expressly incorporated by reference herein.

[0019] A. Definitions

[0020] Amino Acid Residue: An amino acid formed upon chemical digestion (hydrolysis) of a polypeptide at its peptide linkages. The amino acid residues described herein are preferably in the "L" isomeric form. However, residues in the "D" isomeric form can be substituted for any L-amino acid residue, as long as the desired functional property is retained by the polypeptide. NH₂ refers to the free amino group present at the amino terminus of a polypeptide. COOH refers to the free carboxy group present at the carboxy terminus of a polypeptide. The standard polypeptide nomenclature (described in *J. Biol. Chem.*, 243:3552-59

(1969) and adopted at 37 CFR §1.822(b)(2)) that provides one letter and three letter codes for amino acid residues is used.

[0021] It should be noted that all amino acid residue sequences represented herein by formulae have a left-to-right orientation in the conventional direction of amino terminus to carboxy terminus. In addition, the phrase "amino acid residue" is broadly defined to include modified and unusual amino acids, such as those listed in 37 CFR 1.822(b)(4), and incorporated herein by reference. Furthermore, it should be noted that a dash at the beginning or end of an amino acid residue sequence indicates a peptide bond to a further sequence of one or more amino acid residues or a covalent bond to an amino-terminal group such as NH₂ or acetyl or to a carboxy-terminal group such as COOH.

[0022] Recombinant DNA molecule: a DNA molecule produced by operatively linking two DNA segments. Thus, a recombinant DNA molecule is a hybrid DNA molecule comprising at least two nucleotide sequences not normally found together in nature.

[0023] Receptor: A receptor is a molecule, such as a protein, glycoprotein and the like, that can specifically (non-randomly) bind to another molecule.

[0024] Antibody: The term antibody in its various grammatical forms is used herein to refer to immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, i.e., molecules that contain an antibody combining site or paratope. Exemplary antibody molecules are intact immunoglobulin molecules, substantially intact immunoglobulin molecules and portions of an immunoglobulin molecule, including those portions known in the art as Fab, Fab', and F(ab')₂.

[0025] Antibody Combining Site: An antibody combining site is that structural portion of an antibody molecule comprised of a heavy and light chain variable and hypervariable regions that specifically binds (immunoreacts with) an antigen. The term immunoreact in its various forms means specific binding between an antigenic determinant-containing molecule and a molecule containing an antibody combining site such as a whole antibody molecule or a portion thereof.

[0026] Monoclonal Antibody: A monoclonal antibody in its various grammatical forms refers to a population of antibody molecules that contain only one species of antibody combining site capable of immunoreacting with a particular epitope. A monoclonal antibody thus typically displays a single binding affinity for any epitope with which it immunoreacts. A monoclonal antibody may therefore contain an antibody molecule having a plurality of antibody combining sites, each immunospecific for a different epitope, e.g., a bispecific monoclonal antibody.

[0027] Upstream: In the direction opposite to the direction of DNA transcription, and therefore going from 5' to 3' on the non-coding strand, or 3' to 5' on the mRNA.

[0028] Downstream: Further along a DNA sequence in the direction of sequence transcription or read out, that is traveling in a 3'- to 5'-direction along the non-coding strand of the DNA or 5'- to 3'-direction along the RNA transcript.

[0029] Polypeptide: A linear series of amino acid residues connected to one another by peptide bonds between the alpha-amino group and carboxy group of contiguous amino acid residues.